## REMARKS

Claims 33-42 are pending in the instant application. By this amendment, Claims 33-34, 37-39 and 41-42 have been amended to address the Examiner's concerns in the Office Action and to present the rejected claims in condition for allowance and/or in better form for consideration on appeal. In particular, Claims 33-34, 39 and 41-42 have been amended to replace the phrase "preventing the initiation, development, or progression of melanoma" with "inhibiting the development or progression of melanoma." Support for these claim amendments may be found throughout the specification, see, *e.g.*, at page 1, lines 3-6; page 15, lines 9-13; page 17, lines 15-20; and page 20, lines 14-15. In addition, Claims 37-39 have been amended to remove the specific reference to small molecule inhibitors. Applicants reserve the right to prosecute claims to any cancelled subject matter in this application or one or more continuation, continuation-in-part, or divisional applications.

Thus, upon entry of the present amendments, claims 33-42 will be pending and under consideration.

### The Rejections Under 35 U.S.C. § 112, Second Paragraph, Should Be Withdrawn

Claims 37-40 and 42 were rejected under 35 U.S.C. § 112, second paragraph for indefiniteness. The Office Action asserts that the term "small molecule inhibitor" is indefinite because the art does not provide a limiting definition of the term "small". In response, Claims 37-39 have been amended to remove the phrase "small molecule inhibitor" in order to expedite allowance of the application because such compounds are within the scope of the independent Claims 33 and 34, which have no such restriction on the size of the compound.

Accordingly Applicants respectfully request that the rejections of Claims 37-40 and 42 under 35 U.S.C. § 112, second paragraph, be withdrawn.

### The Rejections Under 35 U.S.C. § 112, First Paragraph, for Lack of Enablement Should Be Withdrawn

Claims 33-42 are rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement. The Office Action asserts that the specification enables a method of inhibiting the development or progression of melanoma comprising administering to a patient in need thereof a compound that is an endothelin B receptor-specific antagonist, it does not provide enablement for a method of preventing the initiation of melanoma using such compounds.

The Examiner asserts that the art teaches that the initiation of cancer is a mutational event, and, although the specification teaches that endothelin B receptor-specific antagonist inhibit the early events associated with melanoma development, it does not provide enablement for the prevention or reversal of a mutational event such that the primary initiation event in melanoma is prevented. The Office Action further asserts that the specification does not teach how to identify "a patient in need thereof" because, prior to such a mutational event that leads to initiation of melanoma, said patient would be without atypical lesions.

In response, Claims 33, 34, 39, 41 and 42, and claims dependent thereon, i.e., Claims 35-38 and 40, have been amended to recite a method for inhibiting the development and progression of melanoma, or of a melanocyte or melanocyte-related cell into a melanoma cell. This amendment clarifies that the claimed methods relate the use of ETB-specific antagonists to inhibit early events in melanoma development and progression resulting from ET signaling, but is not meant to encompass the use of such compounds to prevent mutational events associated with primary events in melanoma initiation.

Thus, Applicants submit that the above amendment overcomes the rejection of Claims 33-42 for lack of enablement. Accordingly, the withdrawal of the rejections of Claims 33-42 for lack of enablement is respectfully requested.

**The Rejections Under 35 U.S.C. § 112, First Paragraph for Lack of Written Description Should Be Withdrawn**

Claims 33-42 are rejected under 35 U.S.C. § 112, first paragraph for lack of written description. According to the Examiner, the art teaches that the initiation of cancer is a mutational event, and the specification does not describe a method of preventing a mutational event such that the primary initiation event in melanoma is prevented.

Applicants submit that the amendment of Claims 33-42 described above obviate this rejection. By this amendment, it is clear that the invention is not intended to encompass the prevention of mutational events. Accordingly, Applicants respectfully request that the rejections of Claims 33-42 for lack of enablement be withdrawn.

Applicants respectfully request that the amendment be entered and the remarks herein be made of record in the file history of the instant application. Applicants estimate that the remarks and amendments made herein now place the pending claims in condition for allowance.

Respectfully submitted,

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